

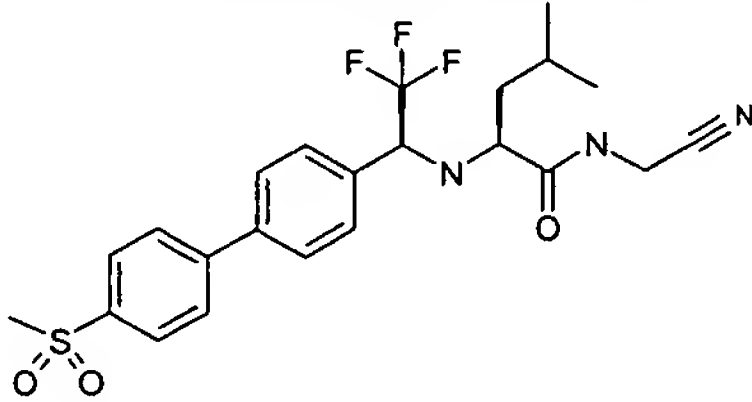
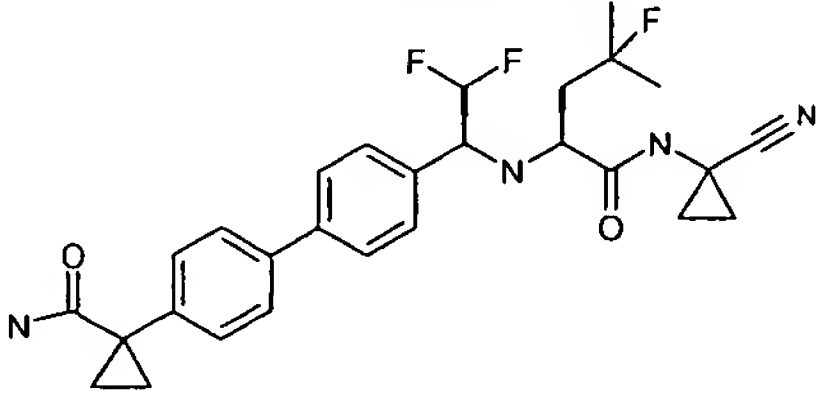
REMARKS

Claims 1-12 are pending in the instant application. Claims 10 and 12 have been withdrawn from consideration and have been cancelled. Claims 1-9 and 11 have been rejected. After entry of these arguments, Claims 1-9 and 11 will remain pending.

Rejection of Claims 1- 7, 9 and 11 under 35 USC §103(a)

The Examiner has rejected Claims 1-7, 9 and 11 under 35 U.S.C. §103(a), as allegedly being unpatentable over Bayly et al. (WO 03/075836). Specifically, the Examiner admits that Bayly et al. do not teach an amide group and E group being separated by an X group, such as a 3-8 membered cycloalkyl or CR^aR^b where R^a and R^b can be hydrogen. The Examiner further admits that "Bayly et al. do not teach specifically a compound where the X group would be present." However, the Examiner argues that Bayly et al. show the person of ordinary skill in the art to modify specific compounds by inserting a linking group to generate another cathepsin inhibitor with a reasonable expectation of success.

Applicants respectfully traverse this rejection. Drug discovery and design is a complex process, and the activity of seemingly similar compounds can be significantly different when tested. Although the compounds of the instant invention are structurally similar to those in Bayly et al., the compounds of the instant invention have improved selectivity over cathepsins S and L, when compared to representative compounds in Bayly et al.:

	<i>REPRESENTATIVE COMPOUND FROM BAYLY ET AL.</i>	<i>COMPOUND OF THE INSTANT INVENTION</i>
<i>Structure</i>		
Enzyme Selectivity: Human Cathepsin L Human Cathepsin S	257 nM 172 nM	5871 nM 694 nM
Cell Selectivity: HepG2 (Cat L) Whole Blood (Cat S)	2810 nM 328 nM	8977 nM 1531 nM

The observed increase in selectivity exhibited by compounds of the instant invention could not have been predicted, and was not taught by Bayly et al.


In light of these arguments, Applicants respectfully request the rejections of Claims 1-9 and 11 under 35 USC §103(a), be withdrawn.

Provisional Double Patenting Rejection

The Examiner has provisionally rejected Claims 1-9 and 11 on the ground of non-statutory obviousness-type double patenting as being unpatentable over at least claims 1 and 15 of copending Application No. 12/082,104. As this rejection is a provisional rejection based upon pending applications which are still undergoing prosecution, and wherein no allowable subject matter has yet been identified, Applicants respectfully request that this rejection be held in abeyance.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

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